

REMARKS

Upon entry of this response, claims 1-28 are still pending in the application. Claim 1 is an independent claim drawn to a micro or nano-particulate drug composition, with claims 2-17 depending therefrom, while claim 18 is an independent claims drawn to a method of making a mirco or nano-particulate drug. The remaining claims (claims 19-28) depend from claim 18. Claims 1, 13 and 24 have been amended to clarify the present inventive subject matter. Support for the claim amendments may be found throughout the specification as originally filed. Thus, Applicant submits that no new matter within the meaning of 35 U.S.C. 132 is added by the amendments to the claims.

Claims 13 and 24 stand rejected under 35 U.S.C. 101 as being directed to non-statutory subject matter, and under 35 U.S.C. 112, first paragraph as being based on a lack of written description; Claims 1-14 and 18-25 stand rejected as being anticipated by WO 99/40943; and Claims 15-17 and 26-28 stand rejected as obvious over WO 99/40943. Claims 13 and 24 are also rejected under 35 U.S.C. 112, second paragraph as being indefinite, as are claims 1-17.

Applicant respectfully traverses these rejection and respectfully request reconsideration and withdrawal thereof. The amendments to the claims and the following remarks are made in order to place the application in condition for allowance.

Rejection of Claims 13 and 24 Under 35 U.S.C. 101 and

35 U.S.C. 112, First Paragraph

Claims 13 and 24 stand rejected under 35 U.S.C. 101 as being directed to non-statutory subject matter for the claiming of the term "natural product," and under 35 U.S.C. 112, first paragraph as being based on a lack of written description over the use of the terms "low molecular weight oligomers, natural products and organic solvents."

RESPONSE

Applicant respectfully traverses this rejection and requests reconsideration and withdrawal thereof.

Applicants have amended claims 13 and 24 to remove the term "low molecular weight oligomers, natural products and organic solvents," thereby removing the basis for these rejections and obviating these rejections. As such, Applicant submits that the claims are now directed to statutory subject matter and the specification now provides proper written description of the inventive subject matter, and requests reconsideration and withdrawal of the rejection.

Rejection of Claims 1-14 and 18-25 Under 35 U.S.C. 102(b)

Claims 1-14 and 18-25 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/40943 (the '943 reference) for the reasons set forth in the Office Action.

RESPONSE

Applicant respectfully traverses this rejection and respectfully requests reconsideration and withdrawal thereof.

To establish an anticipation rejection, every claimed element must be found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. V. Union Oil Co. of California*, 814 F2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); See also, MPEP § 2131. Applicant respectfully submits that the Examiner has not met this burden with respect to the anticipation rejection.

Briefly, as amended, independent claim 1 is directed to a micro or nano-particulate drug composition in which a surfactant-drug substance matrix is formed **at a temperature above the matrix's melting temperature**, with the matrix comprising a drug substance and a surfactant, and wherein the drug composition further comprises micro or nano-sized crystals of said drug crystals coated the surfactant at room temperature, the crystals being formed while the matrix is cooled to room temperature under

a shearing force. Further, independent claim 18 includes the limitations of melting a drug substance-surfactant mixture **at a temperature above said mixture's melting temperature**, and cooling the mixture under high shear to approximately room temperature, wherein crystals precipitate coated with the surfactant during crystallization. The remaining claims depend from the independent claims and therefore contain all of the limitations found therein, including those discussed above. Applicant respectfully submits that the '943 reference fails to teach these limitations, and thus does not anticipate claims 1-14 and 18-25.

The '943 reference discloses delivery systems in which active agent/surfactant combinations are blended using selected processing conditions. Applicants respectfully submit that the '943 reference is concerned with coating **solid particles** of the active agent with a eutectic mixture of active agent and solubilizer. For example, on page 2, lines 21-26, the '943 reference states that "the invention relates to solubilizing delivery systems and the method of producing them wherein particles of at least one active agent and at least one solubilizing agent, such as surface active agents (solubilizer), are processed at low temperatures, i.e. **at temperatures below the melting points of both, and preferably from below the formation of a eutectic of the active and solubilizer**

combination to below the temperature at which the active dissolves in the solubilizer." (Emphasis added). Thus, it can be seen that the delivery system and process of the '943 patent involves forming a combination by processing active agent particles with a solubilizer **at a temperature below the melting points of both ingredients.** In other words, the active particles and the solubilizer are **not** melted together.

The '943 reference continues, at page 3, lines 10-11, by stating that "these eutectics (active agents and solubilizers), while in the presence of the temperature and force, **will coat or envelop, at least partially, particles of the active.** (Emphasis added). In addition, the '943 reference states, at page 6, lines 15-23, that "the method of the invention involves contacting **solid particles of the active,** including drug, and the solubilizer under conditions suitable to form the delivery system products of the invention....Preferably the temperatures at which the ingredients are contacted are from below the formation point of the combination's eutetic to below the temperature at which the active will dissolve in the solubilizer **so that the drug does not totally dissolve in the eutectic."** (Emphasis added).

Thus, it can be seen that the '943 reference is concerned with coating solid particles of the active drug with the eutectic

mixture and does not disclose the **claimed matrix** which is formed at a temperature **above the melting point of the matrix**, i.e., all of the ingredients in the present inventive subject matter are at some point in liquid form. Further, the '943 reference does not disclose the claimed product and process by which the crystals **are formed or grown** by cooling the matrix to room temperature under a shear force. In other words, the currently claimed product is the result of shearing the melted matrix while cooling, which results in the crystals growing from the melted matrix. Applicant submits that this is a different process than that disclosed in the '943 reference.

In summary, Applicant respectfully submits that the '943 reference fails to disclose the limitations of a matrix from at a temperature above its melting temperature and crystal coated with surfactant which are grown by shearing the melted matrix while cooling to room temperature. As such, Applicant submits that the '943 reference fails to disclose all of the limitations of independent claims 1 and 18, and therefore also of the claims that depend therefrom.

Accordingly, Applicant submits that the '943 reference does not anticipate the claims, and respectfully requests reconsideration and withdrawal of this rejection.

Rejection of Claims 15-17 and 26-28 Under 35 U.S.C. 103(a)

Claims 15-17 and 26-28 stand rejected under 35 U.S.C. 103(a) as being obvious over WO 97/40943 (the '943 reference) for the reasons set forth in the Office Action.

RESPONSE

Applicant respectfully traverses this rejection and requests reconsideration and withdrawal thereof.

The reference of record, the '943 reference, does not teach or suggest Applicant's inventive subject matter as a whole, as recited in the claims. Further, there is no teaching or suggestion in this reference which would lead the ordinary skilled artisan to modify the reference to derive the subject matter as defined in the amended claims.

The U.S. Supreme Court in *Graham v. John Deere Co.*, 148 U.S.P.Q. 459 (1966) held that non-obviousness was determined under § 103 by (1) determining the scope and content of the prior art; (2) ascertaining the differences between the prior art and the claims at issue; (3) resolving the level of ordinary skill in the art; and, (4) inquiring as to any objective evidence of nonobviousness.

To establish a *prima facie* case of obviousness, the Examiner must establish: (1) that some suggestion or motivation to modify the references exists; (2) a reasonable expectation of success; and (3) that the prior art references teach or suggest all the claim limitations. Amgen, Inc. v. Chugai Pharm. Co., 18 USPQ2d 1016, 1023 (Fed. Cir. 1991); In re Fine, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988); In re Wilson, 165 USPQ 494, 496 (C.C.P.A. 1970).

A *prima facie* case of obviousness must also include a showing of the reasons why it would be obvious to modify the references to produce the present invention. See Ex parte Clapp, 277 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). The Examiner bears the initial burden to provide some convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings. Id. at 974. Applicant respectfully submits that the Examiner has failed to meet this burden.

Claims 15-17 and 26-28 depend from independent claims 1 and 18, respectively, and therefore necessarily contain all of the limitations found therein. Thus, if claims 1 and 18 are not obvious over the '943 reference, then neither are claims 15-17 and 26-28.

As is indicated above in the response to the anticipation rejection, independent claim 1 is directed to a micro or

nano-particulate drug composition in which a surfactant-drug substance matrix is formed **at a temperature above the matrix's melting temperature**, with the matrix comprising a drug substance and a surfactant, and wherein the drug composition further comprises micro or nano-sized crystals of said drug crystals coated the surfactant at room temperature, the crystals being formed while the matrix is cooled to room temperature under a shearing force. Further, independent claim 18 includes the limitations of melting a drug substance-surfactant mixture **at a temperature above said mixture's melting temperature**, and cooling the mixture under high shear to approximately room temperature, wherein crystals precipitate coated with the surfactant during crystallization. The remaining claims depend from the independent claims and therefore contain all of the limitations found therein, including those discussed above. Applicant respectfully submits that the '943 reference fails to teach these limitations, and thus does not anticipate claims 1-14 and 18-25.

The '943 reference discloses delivery systems in which active agent/surfactant combinations are blended using selected processing conditions. Applicant respectfully submits that the '943 reference is concerned with coating **solid particles** of the active agent with a eutectic mixture of active agent and solubilizer. For example, on page 2, lines 21-26, the '943 reference states that "the

invention relates to solubilizing delivery systems and the method of producing them wherein particles of at least one active agent and at least one solubilizing agent, such as surface active agents (solubilizer), are processed at low temperatures, i.e. **at temperatures below the melting points of both, and preferably from below the formation of a eutectic of the active and solubilizer combination to below the temperature at which the active dissolves in the solubilizer.**" (Emphasis added). Thus, it can be seen that the delivery system and process of the '943 patent involves forming a combination by processing active agent particles with a solubilizer **at a temperature below the melting points of both ingredients.** In other words, the active particles and the solubilizer are **not** melted together.

The '943 reference continues, at page 3, lines 10-11, by stating that "these eutectics (active agents and solubilizers), while in the presence of the temperature and force, **will coat or envelop, at least partially, particles of the active.**" (Emphasis added). In addition, the '943 reference states, at page 6, lines 15-23, that "the method of the invention involves contacting **solid particles of the active,** including drug, and the solubilizer under conditions suitable to form the delivery system products of the invention....Preferably the temperatures at which the ingredients

are contacted are from below the formation point of the combination's eutectic to below the temperature at which the active will dissolve in the solubilizer **so that the drug does not totally dissolve in the eutectic.**" (Emphasis added).

Thus, it can be seen that the '943 reference is concerned with coating solid particles of the active drug with the eutectic mixture and does not disclose the **claimed matrix** which is formed at a temperature **above the melting point of the matrix**, i.e., all of the ingredients in the present inventive subject matter are at some point in liquid form. Further, the '943 reference does not disclose the claimed product and process by which the crystals **are formed or grown** by cooling the matrix to room temperature under a shear force. In other words, the currently claimed product is the result of shearing the melted matrix while cooling, which results in the crystals growing from the melted matrix. Applicant submits that this is a different process than that disclosed in the '943 reference.

In summary, Applicant respectfully submits that the '943 reference fails to disclose the limitations of a matrix from at a temperature above its melting temperature and crystal coated with surfactant which are grown by shearing the melted matrix while cooling to room temperature. As such, Applicant submits that the '943 reference fails to disclose all of the limitations of

independent claims 1 and 18, and therefore also of the claims that depend therefrom, including claims 15-17 and 26-28, respectively.

In addition, Applicant respectfully submits that one of ordinary skill in the art would not be led by the '943 reference to attempt cooling the melted mixture under high shear. As is stated above, the '943 reference is directed to coating solid particle with the eutectic mixture, not of growing crystals from the melted matrix. No mention is made in the reference regarding the need to continue applying a high shear rate **as the melted mixture is cooled** in order to form the crystals, since the reference teaches coating solid particles. Therefore, there is no motivation for a skilled artisan to continue applying the high shear rate as the mixture is cooled.

Therefore, Applicants respectfully submit that the '943 reference fails to teach each and every claimed limitation in the independent claims (and also the dependent claims), and that there is no motivation within the patent to modify it in an attempt to achieve the presently claimed subject matter. Thus, the Examiner has failed to meet the burden of proving a *prima facie* case of obviousness.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of the claims as being obvious over the '943 reference.

Rejection of claims 1-17 Under
35 U.S.C. 112, Second Paragraph

Claims 1-17 stand rejected under 35 U.S.C. 112, second paragraph as being indefinite for the reasons set forth in the Office Action.

RESPONSE

Applicant respectfully traverses this rejection and requests reconsideration and withdrawal thereof.

Applicant has amended claim 1 to make clear that the inventive subject matter is directed to a surfactant-drug substance matrix formed at a temperature above said matrix's melting temperature and that the drug crystals are coated with the surfactant. Applicant submits that the amendments to claim 1 obviate this rejection, and therefore request reconsideration and withdrawal thereof.

CONCLUSION

In view of the foregoing, applicants respectfully request the Examiner to reconsider and withdraw the all pending rejections, and to allow all of the claims pending in this application.

If the Examiner has any questions or comments regarding this

Attorney Docket: 24720
Serial No. 10/022,799
Filed: December 20, 2001

matter, he is welcomed to contact the undersigned attorney at the below-listed number and address.

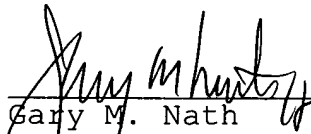
Respectfully submitted,
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Date:

February 4, 2005

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